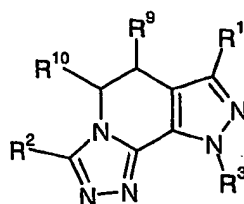


Claims

1. An inhaled combination of (a) a selective PDE4 inhibitor of the formula (I)

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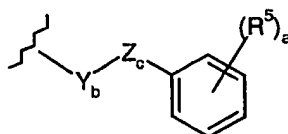


(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein:

- 10 R¹ is H, (C₁-C₆) alkyl, (C₁-C₆) alkoxy, (C₂-C₄) alkenyl, phenyl, -N(CH₃)₂, (C₃-C₆) cycloalkyl, (C₃-C₆) cycloalkyl(C₁-C₃) alkyl or (C₁-C₆) acyl, wherein the alkyl, phenyl or alkenyl groups may be substituted with up to two -OH, (C₁-C₃) alkyl, or -CF₃ groups or up to three halogens;

- R² and R³ are each independently selected from the group consisting of H,
 15 (C₁-C₁₄) alkyl, (C₁-C₇) alkoxy(C₁-C₇) alkyl, (C₂-C₁₄) alkenyl, (C₃-C₇) cycloalkyl, (C₃-C₇) cycloalkyl(C₁-C₂) alkyl, a saturated or unsaturated (C₄-C₇) heterocyclic(CH₂)_n group wherein n is 0, 1 or 2, containing as the heteroatom one or two of the group consisting of oxygen, sulfur, sulfonyl, nitrogen and NR⁴ where R⁴ is H or (C₁-C₄) alkyl; or a group of the Formula (II):



(II)

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- wherein a is an integer from 1 to 5; b and c are 0 or 1; R⁵ is H, -OH, (C₁-C₅) alkyl, (C₂-C₅) alkenyl, (C₁-C₅) alkoxy, (C₃-C₆) cycloalkoxy, halogen, -CF₃, -CO₂R⁶, -CONR⁶R⁷, -NR⁶R⁷, -NO₂, or -SO₂NR⁶R⁷ wherein R⁶ and R⁷ are each
 25 independently H, or (C₁-C₄) alkyl; Z is -O-, -S-, -SO₂-, -CO- or -N(R⁸)- wherein R⁸ is H or (C₁-C₄) alkyl; and Y is (C₁-C₅) alkylene or (C₂-C₆) alkenylene optionally substituted with up to two (C₁-C₇) alkyl or (C₃-C₇) cycloalkyl groups; wherein each

of the alkyl, alkenyl, cycloalkyl, alkoxyalkyl or heterocyclic groups may be substituted with 1 to 14, preferably 1 to 5, (C₁-C₂) alkyl, CF₃, or halo groups; and R⁹ and R¹⁰ are each independently selected from the group consisting of H, (C₁-C₆) alkyl, (C₁-C₆) alkoxy, (C₆-C₁₀) aryl and (C₆-C₁₀) aryloxy;

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and (b) an adrenergic β₂ receptor agonist.

2. A combination as claimed in claim 1 wherein R¹ is methyl, ethyl or isopropyl.

3. A combination as claimed in claim 1 or claim 2 wherein R³ is (C₁-C₆) alkyl, (C₂-C₆) alkenyl, (C₃-C₇) cycloalkyl, (C₃-C₇)cycloalkyl(C₁-C₆)alkyl or phenyl
10 optionally substituted with 1 or 2 of the group consisting of H, -OH, (C₁-C₅) alkyl, (C₂-C₅) alkenyl, (C₁-C₅) alkoxy, halogen, trifluoromethyl, -CO₂R⁶, -CONR⁶R⁷, -NR⁶R⁷, -NO₂ or -SO₂NR⁶R⁷ wherein R⁶ and R⁷ are each independently H or (C₁-C₄) alkyl. ✓

15 4. A combination as claimed in any one of the preceding claims wherein the selective PDE4 inhibitor of the formula (I) is selected from:

9-cyclopentyl-5,6-dihydro-7-ethyl-3-phenyl-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(furan-2-yl)-9H-pyrazolo[3,4-c]-1,2,4-
20 triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-pyridyl)-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(4-pyridyl)-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine;

25 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(3-thienyl)-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine;

3-benzyl-9-cyclopentyl-5,6-dihydro-7-ethyl-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-propyl-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-
30 α]pyridine;

- 3,9-dicyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine;
- 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine;
- 5 3-(*tert*-butyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine;
- 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine;
- 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methoxyphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-
- 10 triazolo[4,3- α]pyridine;
- 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(thien-2-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine;
- 3-(2-chlorophenyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine;
- 15 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-iodophenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine;
- 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-trifluoromethylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine; and
- 5,6-dihydro-7-ethyl-9-(4-fluorophenyl)-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine;
- 20 *c*]-1,2,4-triazolo[4,3- α]pyridine;
- and the pharmaceutically acceptable salts and solvates thereof.
5. A combination as claimed in claim 4 wherein the selective PDE4 inhibitor of the formula (I) is selected from 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine and 9-cyclopentyl-5,6-dihydro-7-
- 25 ethyl-3-(*tert*-butyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine and the pharmaceutically acceptable salts and solvates thereof.
6. A combination as claimed in any one of the preceding claims wherein the adrenergic β 2 receptor agonist is selected from salmeterol, formoterol and the pharmaceutically acceptable salts and solvates thereof.
- 30 7. A combination as claimed in claim 1 wherein:

- the selective PDE4 inhibitor of the formula (I) is 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine, or a pharmaceutically acceptable salt or solvate thereof, and the adrenergic β 2 receptor agonist is salmeterol, or a pharmaceutically acceptable salt or solvate thereof;
- the selective PDE4 inhibitor of the formula (I) is 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine, or a pharmaceutically acceptable salt or solvate thereof, and the adrenergic β 2 receptor agonist is formoterol, or a pharmaceutically acceptable salt or solvate thereof;
- the selective PDE4 inhibitor of the formula (I) is 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(*tert*-butyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine, or a pharmaceutically acceptable salt or solvate thereof, and the adrenergic β 2 receptor agonist is salmeterol, or a pharmaceutically acceptable salt or solvate thereof; or
- the selective PDE4 inhibitor of the formula (I) is 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(*tert*-butyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- α]pyridine, or a pharmaceutically acceptable salt or solvate thereof, and the adrenergic β 2 receptor agonist is formoterol, or a pharmaceutically acceptable salt or solvate thereof.
8. A combination as claimed in any preceding claim for use as a medicament.
9. A combination as claimed in any one of claims 1 to 7 for simultaneous, sequential or separate administration in the treatment of an obstructive airways or other inflammatory disease.
10. A pharmaceutical composition comprising a selective PDE4 inhibitor of the formula (I), as defined in claim 1, an adrenergic β 2 receptor agonist and a pharmaceutically acceptable excipient, diluent or carrier, for administration by the inhaled route in the treatment of an obstructive airways or other inflammatory disease.

11. A pharmaceutical composition as defined in claim 10 wherein the selective PDE4 inhibitor of the formula (I) and the adrenergic β 2 receptor agonist are as defined in any one of claims 2 to 7.
12. The use of a selective PDE4 inhibitor of the formula (I), as defined in claim 5 1, or an adrenergic β 2 receptor agonist in the manufacture of a medicament for simultaneous, sequential or separate administration of both agents by the inhaled route in the treatment of an obstructive airways or other inflammatory disease.
13. The use of claim 12 wherein the selective PDE4 inhibitor of the formula (I) 10 and the adrenergic β 2 receptor agonist are as defined in any one of claims 2 to 7.
14. A method of treating of an obstructive airways or other inflammatory disease comprising administering simultaneously, sequentially or separately, by the inhaled route, to a mammal in need of such treatment, an effective amount of 15 a selective PDE4 inhibitor of the formula (I), as defined in claim 1, and an adrenergic β 2 receptor agonist.
15. A method as claimed in claim 14 wherein the selective PDE4 inhibitor of the formula (I) and the adrenergic β 2 receptor agonist are as defined in any one of claims 2 to 7.
- 20 16. An inhalation device for simultaneous, sequential or separate administration of a selective PDE4 inhibitor of the formula (I), as defined in claim 1, and an adrenergic β 2 receptor agonist in the treatment of an obstructive airways or other inflammatory disease.
17. An inhalation device as claimed in claim 16 wherein the selective PDE4 25 inhibitor of the formula (I) and the adrenergic β 2 receptor agonist are as defined in any one of claims 2 to 7.